

Effects of Energy and Carbohydrate Intake on Serum High-Density Lipoprotein-Cholesterol Levels

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Abstract

High-density lipoprotein (HDL) is a lipoprotein which has anti-atherogenic property by reverse cholesterol transport from the peripheral tissues to liver. Low HDL-cholesterol (HDL-C) level is associated with the development of coronary artery diseases. We previously studied effects of energy and carbohydrate intake on serum HDL-C to make “Dietary Reference Intakes for Japanese 2015”, and reported the results by reviewing papers by 2012. Here we review meta-analyses about the effects of energy and carbohydrate intake on serum HDL-C levels which were published from 2012 to 2018, to make “Dietary Reference Intake for Japanese 2020”, by using PubMed, Embase and Google Scholar. Effects of energy restriction on HDL-C may depend on backgrounds of subjects studied, the ratio of carbohydrate, protein and fat. Low carbohydrate diet may increase HDL-C, which may be due to reduction of body weight and/or amelioration of insulin resistance. Regarding intake of free sugar, further studies including effects of free sugar intake on other risk factors in addition to HDL-C should be performed. Fructose intake may exert no effect on HDL-C; however, the fructose intake ≤ 100 g/day may be recommended considering unfavorable effects on triglyceride (TG) and low-density lipoprotein-cholesterol (LDL-C).

Keywords: Body weight; Carbohydrate; Free sugar; Fructose; High-density lipoprotein

Introduction

High-density lipoprotein (HDL) plays a role in reverse cholesterol transport from the peripheral tissues to liver, suppressing cholesterol accumulation in the peripheral tissue. Therefore, serum low HDL-cholesterol (HDL-C) level was considered to be one of risk factors for coronary artery diseases [1, 2].

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We previously studied effects of energy and carbohydrate intake on serum HDL-C levels to make “Dietary Reference Intakes for Japanese 2015”, and reported the results by reviewing papers by 2012 [3]. Here we review articles about the effects of energy and carbohydrate intake on serum HDL-C levels which were published from 2012 to 2018, to make “Dietary Reference Intake for Japanese 2020”.

Methods

To make “Dietary Reference Intake for Japanese 2020”, we searched meta-analyses of randomized controlled trials (RCTs) which have the highest evidence level. A search was conducted by using PubMed, Embase and Google Scholar, with the following keywords: high-density lipoprotein-cholesterol (HDL-C) and energy intake and meta-analysis or high-density lipoprotein-cholesterol (HDL-C) and carbohydrate intake and meta-analysis. The search period was comprised between January 2012 and March 2018.

Results

Effects of energy intake on HDL-C

We found three meta-analyses which studied effects of energy intake on HDL-C. Parretti et al conducted a meta-analysis of very-low-energy diets (VLEDs) used to treat obesity, by using RCTs included where the intervention included an VLED and the comparator was no intervention or an intervention that could be given in a general medical setting in adults that were overweight [4]. Compared with a behavioral program alone, VLEDs combined with a behavioral program achieved -3.9 kg (95% confidence interval (CI): -6.7 to -1.1) at 1 year. An increase of HDL-C of 0.06 mmol/L (95% CI: 0.00 , 0.13 mmol/L) was obtained.

In the systematic review with meta-analysis which assessed the effect of diet on changes in parameters describing the body size phenotype of metabolically healthy obese subjects, the combined analyzed population consists of 1,827 subjects aged 34.4 to 61.1 with a body mass index (BMI) of > 30 kg/m² [5]. Time of intervention ranged from 8 to 104 weeks. This systematic review revealed a significant association between restricted energy diet and BMI (-2.70 kg/m²; 95% CI: -4.01 , -1.39), triglyceride (TG) (-0.11 mmol/L; 95% CI: -0.16 ,

-0.06). However, a significant association between restricted energy diet and HDL-C could not be observed.

A systematic review and meta-analysis of studies that compared energy-restricted, isocaloric, high-protein, low-fat (HP) diets with standard-protein, low-fat (SP) diets on cardiometabolic risk factors was conducted [6]. Compared with an SP diet, an HP diet produced more favorable changes in weighted mean differences for reductions in body weight, fat mass, and TG. However, HDL-C was similar across dietary treatments.

Effects of carbohydrate intake on HDL-C

Meta-analyses evaluated effects of carbohydrate intake on HDL-C as shown in Table 1 [7-13]. Seven meta-analyses were eligible. Only one meta-analysis failed to prove that low-carbohydrate diet increases HDL-C. However, six meta-analyses showed that low-carbohydrate diet significantly increased serum HDL-C levels.

Effects of sugar intake on HDL-C

Meta-analyses evaluated effects of sugar intake on HDL-C as shown in Table 2 [14-17]. Four meta-analyses were eligible.

When free sugars were substituted for complex carbohydrates, a significant increase in HDL was observed [14]. However, in another systematic review and meta-analysis of RCTs that examined effects of the modification of dietary free sugars on lipids, higher compared with lower sugar intakes significantly raised HDL-C [15].

In a meta-analysis which searched through July 7, 2015 for controlled feeding trials with follow-up ≥ 7 days, which investigated the effect of oral fructose compared to a control carbohydrate on lipids, fructose had no effect on HDL-C in isocaloric trials [16]. In a systematic review and meta-analysis of human, controlled, feeding trials involving isocaloric fructose exchange for other carbohydrates to quantify the effects of fructose on serum lipids in adult humans, fructose exerted no effect on HDL-C [17].

Discussion

In addition to decreased HDL-C, elevation of TG is commonly observed in an insulin-resistant state such as obesity, metabolic syndrome and type 2 diabetes [18]. Reduction of body weight increases HDL-C and decreases TG. Therefore, we evaluated effects of energy, carbohydrate and sugar intake on body weight and other serum lipids in addition to HDL-C.

One meta-analysis showed a significant association between energy restriction and body weight and TG, however, failed to show a significant association between energy restriction and HDL-C in metabolically healthy obese subjects [5]. Another meta-analysis using overweight adults who were not always defined as metabolically healthy, showed significant improvement of body weight and HDL-C [4]. Energy-restrict-

ed, isocaloric, high-protein, low-fat diets did not make a difference in HDL-C as compared with standard-protein, low-fat diets [6]. Effects of energy restriction on HDL-C may vary by backgrounds of subjects, the ratio of carbohydrate, protein and fat intake.

The low carbohydrate diet, in which carbohydrates are replaced by greater intake of fat and/or protein, is a popular weight-loss option compared with the conventional low-fat diet. However, concerns have been raised with regard to the macronutrient shift with an extreme carbohydrate restriction and the liberal intakes of fats, which may present detrimental effects on cardiovascular risk factors [19].

In present review, although six meta-analyses showed that low-carbohydrate diet significantly increased HDL-C, only one meta-analysis did not show beneficial effect of low-carbohydrate diet on HDL-C.

Naude et al compared the effects of low carbohydrate and isoenergetic balanced weight loss diets on overweight and obese adults assessed in RCTs [8]. In non-diabetic and diabetic participants, little or no difference was detected at 3 - 6 months and 1 - 2 years for HDL-C. They suggested that there is probably little or no difference in weight loss and changes in cardiovascular risk factors up to 2 years of follow-up when overweight and obese adults, with or without type 2 diabetes, are randomized to low-carbohydrate diets and isoenergetic balanced weight loss diets.

Four of six studies which showed an increase of HDL-C by low-carbohydrate diet demonstrated a significant reduction of both body weight and TG. In the meta-analysis by Ajala et al, reduction of body weight was observed; however, data about TG were not available [10]. The meta-analysis by Huntriss et al showed statistical significance in favor of the low-carbohydrate intervention arm for TG; however, body weight did not demonstrate a statistically significant difference between interventions [11]. Low-carbohydrate diet may increase HDL-C, which may be due to body weight reduction and/or improvement of insulin resistance.

In a meta-analysis of RCTs to compare diets that provide a given amount of energy from free sugars with a control diet that provides the same amount of energy from complex carbohydrates, a significant increase in HDL-C was observed; however, significant increases in LDL-C and TG were also observed [14]. In another meta-analysis, higher compared with lower sugar intakes significantly raised HDL-C, TG and LDL-C [15]. Regarding the effect of free sugar intake on HDL-C, two meta-analyses showed the opposite result. However, both studies showed that free sugar intake was significantly associated with an increase of TG and LDL-C. Further studies including effects of free sugar on other risk factors in addition to HDL-C should be performed in the future.

Two meta-analyses showed no effect of fructose intake on HDL-C [16, 17]. There were no effects of fructose intake on LDL-C, non-HDL-C, apolipoprotein B, and TG in isocaloric trials. However, in hypercaloric trials, fructose increased apolipoprotein B and TG [16]. Isocaloric fructose exchange for carbohydrates increased LDL-C at > 100 g fructose/day [17]. However, no effect was shown on LDL-C when the fructose intake was ≤ 100 g/day. Fructose intake may exert no effect on HDL-C; however, the fructose intake ≤ 100 g/day may

Table 1. Meta-Analyses Evaluated Effects of Carbohydrate Intake on HDL-C

Authors	Assessed studies	Subjects studied	Effects on HDL-C	Effects on other lipids	Effects on body weight, body composition
Mansoor et al [7]	RCTs assessing the effects of low-carbohydrate (LC) diets vs. low-fat (LF) diets on weight loss and risk factors. The dietary intervention had a duration of 6 months or longer	11 RCTs with 1,369 participants	Compared with LF diets, LC diets showed a greater increase in HDL-C (WMD: 0.14 mmol/L; 95% CI: 0.09, 0.19)	Compared with LF diets, LC diets showed a greater reduction in TG (WMD: -0.26 mmol/L; 95% CI: -0.37, -0.15), but a greater increase in LDL-C (WMD: 0.16 mmol/L; 95% CI: 0.003, 0.33)	Compared with LF diets, LC diets showed a greater reduction in body weight (WMD: -2.17 kg; 95% CI: -3.36, -0.99)
Nauade et al [8]	Effect of changes in carbohydrate and fatty acid intake on serum lipid and lipoprotein levels	19 trials were included (n=3,209)	Little or no difference was detected at 3 - 6 months and 1 - 2 years for HDL-C	Little or no difference was detected at 3 - 6 months and 1 - 2 years for LDL-C, TC and TG	Little or no difference in mean weight loss in the two groups at 3 - 6 months and 1 - 2 years
Bueno et al [9]	Individuals assigned to a very-low-carbohydrate ketogenic diet (VLCKD) (a diet with no more than 50 g carbohydrates/day) achieve better long-term body weight and cardiovascular risk factor management when compared with individuals assigned to a conventional low-fat diet	13 studies	Individuals assigned to a VLCKD showed increased HDL-C (WMD: 0.09; 95% CI: 0.06, 0.12 mmol/L; 1,257 patients)	Individuals assigned to a VLCKD showed decreased TG (WMD: 20.18; 95% CI: 20.27, 20.08 mmol/L; 1,258 patients) and LDL-C (WMD: 0.12; 95% CI: 0.04, 0.2 mmol/L; 1,255 patients)	Individuals assigned to a VLCKD showed decreased body weight (WMD: 20.91; 95% CI: 21.65, 20.17 kg; 1,415 patients)
Ajala et al [10]	RCTs with interventions that lasted ≥ 6 months that compared low-carbohydrate, vegetarian, vegan, low-glycemic index (GI), high-fiber, Mediterranean, and high-protein diets with control diets including low-fat, high-GI, American Diabetes Association, European Association for the Study of Diabetes, and low-protein diets, in patients with type 2 diabetes	20 RCTs were included (n = 3,073 included in final analyses across 3460 randomly assigned individuals)	An increase in HDL-C was seen in the low-carbohydrate, low-GI, Mediterranean diets	NA	Low-carbohydrate and Mediterranean diets led to greater weight loss (-0.69 kg (P = 0.21) and -1.84 kg (P < 0.00001), respectively)
Huntriss et al [11]	RCTs were searched for which included adults with type 2 diabetes aged 18 years or more. The intervention was a low-carbohydrate diet as defined by the author compared to a control group of usual care	18 studies (n = 2,204)	The meta-analyses showed statistical significance in favor of the low-carbohydrate intervention arm (LCIA) for HDL-C (estimated effect: 0.06 mmol/L; 95% CI: 0.04, 0.09; P < 0.00001)	The meta-analyses showed statistical significance in favor of the LCIA for TG (estimated effect: -0.24 mmol/L; 95% CI: -0.35, -0.13; P < 0.0001). Meta-analyses for TC and LDL-C did not demonstrate a statistically significant difference between interventions	Meta-analyses for weight did not demonstrate a statistically significant difference between interventions
Meng et al [12]	RCTs assessed the efficacy of low carbohydrate diet (LCD) compared with a normal or high carbohydrate diet in patients with type 2 diabetes.	9 studies with 734 patients with diabetes	The LCD intervention significantly increased HDL-C (WMD: 0.07 mmol/L; 95% CI: 0.03, 0.11 mmol/L; P = 0.000)	The LCD intervention significantly reduced TG (WMD: -0.33 mmol/L; 95% CI: -0.45, -0.21 mmol/L; P = 0.00), but, the LCD was not associated with decreased level of TC and LDL-C	Subgroup analyses indicated that short term intervention of LCD was effective for weight loss (WMD: -1.18 kg; 95% CI: -2.32, -0.04 kg; P = 0.04).
Santos et al [13]	Effects of low-carbohydrate diet (LCD) on weight loss and cardiovascular risk factors (search performed on PubMed, Cochrane Central Register of Controlled Trials and Scopus databases)	A total of 23 reports, corresponding to 17 clinical investigations, were identified as meeting the pre-specified criteria. Meta-analysis carried out on data obtained in 1,141 obese patients	LCD was associated with a significant increase in HDL-C (1.73 mg/dL; 95% CI: 1.44, 2.01)	LCD was associated with significant decreases in TG (-29.71 mg/dL; 95% CI: -31.99, -27.44). LDL-C did not change significantly.	LCD was associated with significant decreases in body weight (-7.04 kg; 95% CI: -7.20, -6.88), body mass index (-2.09 kg/m ² ; 95% CI: -2.15, -2.04), abdominal circumference (-5.74 cm; 95% CI: -6.07, -5.41)

BMI: body mass index; CI: confidence interval; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; MD: mean difference; NA: not available; RCT: randomized controlled trial; TC: total cholesterol; TG: triglyceride; WMD: weighted mean difference.

Table 2. Meta-Analyses Evaluated Effects of Sugar Intake on HDL-C

Authors	Assessed studies	Subjects studied	Effects on HDL-C	Effects on other lipids	Effects on body weight, body composition
Fattore et al [14]	RCTs to compare diets that provide a given amount of energy from free sugars with a control diet that provides the same amount of energy from complex carbohydrate	28 studies involving 510 volunteers	A significant increase in HDL-C	Significant increases in LDL-C and TG, although for LDL-C and TG there was significant heterogeneity between studies and evidence of publication bias	The substitution of free sugars for complex carbohydrates had no effect on body weight
Te Morenga et al [15]	Studies that reported intakes of free sugars and at least one lipid or blood pressure outcome. The minimum trial duration was 2 weeks.	39 trials reported lipid outcomes	Higher compared with lower sugar intakes significantly raised HDL-C (MD: 0.02 mmol/L; 95% CI: 0.00, 0.03 mmol/L; P = 0.03).	Higher compared with lower sugar intakes significantly raised TG (MD: 0.11 mmol/L; 95% CI: 0.07, 0.15 mmol/L; P < 0.0001), TC (MD: 0.16 mmol/L; 95% CI: 0.10, 0.24 mmol/L; P < 0.0001), LDL-C (0.12 mmol/L; 95% CI: 0.05, 0.19 mmol/L; P = 0.0001)	Dietary sugars influence serum lipids. The relation is independent of effects of sugars on body weight.
Chiavaroli et al [16]	Controlled feeding trials with follow-up ≥ 7 days, which investigated the effect of oral fructose compared to a control carbohydrate on lipids	51 isocaloric trials (n = 943) and 8 hypercaloric trials (n = 125)	No effect on HDL-C in isocaloric trials	No effect on LDL-C, non-HDL-C, apolipoprotein B, TG in isocaloric trials. In hypercaloric trials, fructose increased apolipoprotein B (n = 2; MD: 0.18 mmol/L; 95% CI: 0.05, 0.30; P = 0.005) and TG (n = 8; MD: 0.26 mmol/L; 95% CI: 0.11, 0.41; P < 0.001).	NA
Zhang et al [17]	Controlled, feeding trials involving isocaloric fructose exchange for other carbohydrates to quantify the effects of fructose on serum TC, LDL-C, and HDL-C in adult humans	24 trials with a total of 474 participants	Fructose exerted no effect on HDL-C	Isocaloric fructose exchange for carbohydrates increased TC by 13.0 mg/dL (95% CI: 4.7, 21.3; P = 0.002) and LDL-C by 11.6 mg/dL (95% CI: 4.4, 18.9; P = 0.002) at >100 g fructose/day. However, no effect was shown on TC or LDL-C when the fructose intake was ≤ 100 g/day	NA

CI: confidence interval; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; MD: mean difference; NA: not available; RCT: randomized controlled trial; TC: total cholesterol; TG: triglyceride.

be recommended considering unfavorable effects of fructose on LDL-C and TG.

Conclusion

Effects of energy restriction on HDL-C may depend on backgrounds of subjects studied and the ratio of macronutrients. Low-carbohydrate diet may increase HDL-C, which may be due to reduction of body weight and/or amelioration of insulin resistance. Further studies including effects of free sugar on other risk factors in addition to HDL-C should be performed in the future. Fructose intake may exert no effect on HDL-C; however, the fructose intake ≤ 100 g/day may be recommended considering unfavorable effects of fructose on other risk factors.

Conflict of Interest

The authors declare that they have no conflict of interest.

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